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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 1203

Application Number: 09/939,689
Filing Date: August 28, 2001
Appellant(s): FRANKS ET AL.

Richard A. Neifeld et al
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed October 29, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

The provisional obviousness-type double patenting rejection set forth in the Office action mailed May 2, 2003, has been overcome by the terminal disclaimer filed July 3, 2003, approved.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 26, 28, 29, 32-34, 38, 39, 41, 43, 46, 47, 52, and 54-68 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

A substantially correct copy of appealed claims 26, 28, 29, 32-34, 38, 39, 41, 43, 46, 47, 52, and 54-68 appears on pages of the Appendix to the appellant's brief. The minor errors are as follows: The text of the claims is correct. However, because this application is a reissue

application and because these claims are new claims with respect to the originally issued patent, the claims on appeal should be underlined, as they were in Applicants' amendments.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

4,824,938 Koyama et al 4-1989

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 38, 39, 41, and 54 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought. The added material which is not supported by the prior patent is as follows: There is no original disclosure supporting the exclusion of rennin as is recited in instant claims 39 and 41. Rennin is not mentioned in the disclosure, and silence in the specification is not support for a negative claim limitation. See Ex parte Grasselli, 231 USPQ 393, aff'd on reconsideration 231 USPQ 395 (Bd. App. 1983). Accordingly, the negative claim limitations in these claims constitute new matter. Claims 38 and 54 recite dissolution in an aqueous solution having a pH of about 7, which embraces dissolution at slightly acidic pHs. However, there is no original disclosure in the specification of dissolution at slightly acidic pHs, the only pHs recited in the sections of the specification cited by Applicants ranging from 7.0 to 7.6. Accordingly, the pH range recited in claims 38 and 54 is new matter.

Claims 38, 39, 41, and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. There is no original disclosure supporting the exclusion of rennin as is recited in instant claims 39 and 41. Rennin is not mentioned in the disclosure, and silence in the specification is not support for a negative claim limitation. See Ex parte Grasselli, 231 USPQ 393, aff'd on reconsideration 231 USPQ 395 (Bd. App. 1983). Claims 38 and 54 recite dissolution in an aqueous solution having a pH of about 7, which embraces dissolution at slightly acidic pHs. However, there is no original disclosure in the specification of dissolution at slightly acidic pHs, the only pHs recited in the sections of the specification cited by Applicants ranging from 7.0 to 7.6. Accordingly, the pH range recited in claims 38 and 54 is not supported by the original disclosure of the invention.

Claims 26, 28, 29, 43, 46, and 52 are rejected under 35 U.S.C. 102(e) as being anticipated by Koyama et al. Koyama et al teach stabilized water-soluble dry solid compositions comprising proteinaceous bioactive substances, for example hormones. Aqueous solutions of the proteinaceous bioactive substances are combined with aqueous solutions a polysaccharide composed mainly of maltotriose units at a ratio of polysaccharide:protein of preferably 1 to 10,000. The weight ratio of the polysaccharide to the substance is at least 0.5, preferably from 1.0 to 10000. The combined solutions are then dried, either by conventional procedures at reduced pressure and a temperature below 30°C, or else by freeze-drying. In one series of examples, greater than 90% of activity is retained after storage at 37°C for one month, which is consistent with Applicants' requirement for at least 53% retained activity after storage for 8 weeks at 25°C. The dry solid can be formed into a tablet and can be used for external or internal administration to prevent or treat human diseases. See, e.g., the Abstract; column 2, lines 10-24 and 38-66; Experiment 3; and the Examples. In view of the similarity in the components of the

compositions and the retained activity of the compositions, the compositions of Koyama et al are deemed inherently to have the same storage stability, and T_g claimed by Applicants and are deemed to anticipate the compositions claimed by Applicants. Sufficient evidence of similarity between the compositions of Koyama et al and Applicants' claimed compositions is deemed to be present to shift the burden to Applicants to show that their claimed compositions are unobviously different than those of Koyama et al. Note that even a patentable difference in the process of making does not necessarily impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art.

Claims 32-34, 47, and 55-68 are rejected under 35 U.S.C. 103(a) as being obvious over Koyama et al as applied against claims 26, 28, 29, 43, 46, and 52 above, and further in view of Applicants' admission of the prior art at column 1, lines 59-62; column 4, lines 57 - 66; and column 5, lines 3-8. Koyama et al do not teach any examples in which conventional drying procedures at reduced pressure and a temperature below 30°C are used. However, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the dried compositions of Koyama et al using conventional drying procedures at reduced pressure and at a temperature below 30°C because as admitted by Koyama et al, such drying procedures are conventional and are suitable for producing Koyama et al's desired products, and because as admitted by Applicants at column 1, lines 59-62, of the application, freeze-drying is costly in capital and energy and is irreproducible. Regardless of the method used to produce the dried compositions of Koyama et al, the dried compositions of Koyama et al would have been expected to have a T_g greater than 20°C because as admitted by Applicants at column 4, lines 59-60, the T_g for maltotriose is 76°C and as admitted by Applicants at column 5, lines 3-8, the T_g for

water-soluble or water-swellable synthetic polymers is a function of molecular weight. Accordingly, the T_g for Koyama et al's polysaccharide composed mainly of maltotriose units would have been expected to be even higher than the 76°C for a maltotriose monomer. The T_g for Koyama et al's proteinaceous bioactive substances would also have been expected to be relatively high because the proteins are also water-soluble polymers of relatively high molecular weight. Even if Koyama et al's dried compositions were to contain several percent residual water after drying, in view of Applicants' admitted rule-of-thumb at column 4, lines 63-65, of an approximately 6°C decrease in T_g for each percent of moisture added, the dried compositions would still have a T_g greater than 20°C in view of the relatively high T_g of the major components. Koyama et al do not teach drying proteins such as enzymes, transport proteins, immunoglobins, and blood clotting factors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to dry proteins such as enzymes, transport proteins, immunoglobins, and blood clotting factors in the methods of Koyama et al because these are known proteinaceous substances which it would be desirable to be able to store and because Koyama et al's method is applicable to all proteinaceous substances which exhibit a bioactivity in vivo.

(11) Response to Argument

Appellants contend: (1) that they were in possession of the genus of claim 39 and 41, either including or excluding renin, and that it should be permissible to exclude renin from the genus where the prior art reference to be distinguished does not teach the generic utility of the claimed invention; (2) that the claimed invention does not have to be literally described in the specification in order to satisfy the new matter and written description requirements, and that the

language "about 7" is a mere rephrasing of what the specification would have conveyed to one of ordinary skill in the art; (3) that Koyama et al do not disclose the actual state of their resulting compositions, and that Koyama et al require freeze drying for all of its experiments and examples; (4) that the examiner's conclusion as to Koyama et al's storage stability and T_g is inconsistent with the disclosure of Koyama et al, namely that because Koyama et al describe their dextran-based compositions as being unstable, they must not have been in a glassy state as required by Appellants' claims; (5) that there is no indication that Koyama et al ever actually performed a conventional drying procedure, and that there were no non-freeze drying conventional drying procedures at the time of Koyama et al; (6) that there is no motivation to perform the process of Koyama et al without freeze drying and that there is no reasonable expectation of success that a stable product in a glassy state would have been produced if such a process had been attempted; (7) that the examiner did not rely upon any teaching suggesting a purified biologically active material which is an immunoglobulin or a blood clotting factor; and (8) that Koyama et al do not suggest evaporation without heating.

With respect to contention (1), the examiner does not have the authority to overrule the case law, including Grasselli. Neither the statute nor the case law indicates that a new matter analysis should take into account what utility is taught by a prior art reference.

With respect to contention (2), the examiner agrees that literal description is not the test for new matter and written description. However, what is disclosed in Appellants' specification are specific examples in which three specific pHs are taught - 7.0, 7.5, and 7.6 (see examples 1-13). The use of the term "about" means that pHs somewhat below 7 are embraced within the

scope of claims 38 and 54, and three specific pHs of 7.0, 7.5, and 7.6 do not convey that Appellants contemplated the acidic pHs embraced by the claim language.

With respect to contention (3), the examiner agrees. However, this does not preclude a rejection based upon inherency for the reasons set forth in the above anticipation rejection.

With respect to contention (4), it is not clear why Appellants' arguments distinguish between Koyama et al's "inventive polysaccharides" and Koyama et al's "ineffective stabilizers". The rejected claims generically recite "a carrier substance that is water-soluble or water-swellable" and embrace Koyama et al's inventive polysaccharides. Accordingly, if the "inventive polysaccharides" of Koyama et al inherently result in the formation of a stable product in a glassy state, Appellants' claim limitations are met regardless of whether or not Koyama et al's "ineffective stabilizers" inherently result in the formation of a stable product in a glassy state. Appellants have not submitted any evidence that the "inventive polysaccharides" of Koyama et al do not inherently result in the formation of a stable product in a glassy state. Secondly, while the examiner agrees that certain "ineffective stabilizers" tested by Koyama et al do not achieve the same stabilizing effect as do Koyama et al's "inventive polysaccharides", this does not mean that the "ineffective stabilizers" of Koyama et al do not meet the stability requirements described by Appellants for their stabilizers. For example, as described by Appellants at page 14 of the Brief, Koyama et al's use of dextran results in 65.3% and 81.5% retention of activity for two months at 37°C and 4°C, respectively. These results, although not sufficient for Koyama et al, are fully consistent with Appellants' disclosed stabilizing effect, e.g., as shown in Example 13, where a stabilizing effect of 53% retention of activity for 8 weeks at 25°C is described. The examiner does not base his inherency argument on comparing the

stabilizing properties of Koyama et al's "ineffective stabilizers" with those of Koyama et al's "inventive polysaccharides"; rather, the inherency argument is based upon comparing the stabilizing properties of Koyama et al's stabilizers with the stabilizing properties of Appellants' claimed carrier substance that is water-soluble or water-swellable. A difference in stabilizing effect amongst Koyama et al's stabilizers does not rebut this inherency argument.

At page 14 of the Brief, Appellants compare the stability achieved by Koyama et al using dextran with the stability achieved by Appellants using dextran. However, these experiments were carried out using different temperatures and times, using different proteins to be stabilized, and using different ratios of protein to stabilizer. This does not constitute a side-by-side comparison of the method of Koyama et al with Appellants' claimed methods, and it is not possible to conclude from these experiments that the method of Koyama et al does not result in the formation of a stable product in a glassy state. A "logical extension of [a] conclusion" is not a basis for determining a residual water concentration of a dried product, and again does not constitute evidence that the dried products of Koyama et al are not stable and/or are not in a glassy state. Appellants have not submitted any probative evidence that Koyama et al do not produce dried compositions in a glassy state, or that Koyama et al's compositions are not storage-stable at 20°C. Accordingly, the inherency argument set forth in the rejection is not rebutted.

With respect to contention (5), the examiner agrees that Koyama et al prefer freeze-drying, and that none of the examples employ evaporative drying. However, the disclosure of a reference is not limited to the reference's examples (In re Snow, 176 USPQ 328 (CCPA 1973)), and a disclosed preferred embodiment does not teach away from nonpreferred embodiments (In

re Susi, 169 USPQ 423 (CCPA 1971)). Further, actual reduction to practice is not a prerequisite for patentability, nor is it a prerequisite for a patent or publication to qualify as prior art under 35 U.S.C. 102 or 103. It is also noted that Koyama et al specifically claim drying the aqueous solution at a temperature below 30°C and reduced pressure (see claim 6), which is further evidence of the obviousness of such a drying step. To the extent that Appellants are arguing that the disclosure of this procedure in Koyama et al is non-enabling, vague, surplusage, etc., all U.S. patents are presumed to be valid, and this presumption includes, e.g., claim 6 of Koyama et al.

Concerning paragraph 39 of the Franks declaration originally filed October 10, 2000, and re-submitted with Appellants' response filed October 3, 2002, this paragraph does not establish how declarant has determined that in 1989 there were no conventional drying procedures carried out at a reduced pressure and a temperature below 30^0C. Also, the declarant limits his statement to the proteinaceous bioactive compound art, whereas the reference's statement could be interpreted as referring to the pharmaceutical drying art or more generally to the drying art. Disclosure in a reference is presumed enabled with the burden being on Appellants to prove non-enablement. Koyama et al's disclosure, and Koyama et al's claims drawn to drying at a temperature below 30^0C and reduced pressure (see claim 6), are not "mere surplusage" just because they may not be supported by any experimental results.

With respect to contention (6), it would have been prima facie obvious to perform the process of Koyama et al without freeze-drying for the reasons set forth in the obviousness rejection, e.g., because such a drying procedure is taught and claimed by Koyama et al to be a conventional useful method of achieving their desired product, and because such a method would have been expected to avoid the capital and energy costs and irreproducibility of freeze-drying.

It would have been expected that the dried products of Koyama et al would be in a glassy state for the reasons set forth in the obviousness rejection, e.g., because of the relatively high T_g's of the components which are dried in Koyama et al's process. It would have been expected that the alternative drying procedure of Koyama et al would result in a biologically active product, because Koyama et al describe the conventional drying procedure carried out at reduced pressure and temperatures below 30°C as being "feasible" and because Koyama et al claim such procedures (see claim 6).

Appellants' arguments at pages 17 and 18 of the Brief that drying without freezing "would destroy an unacceptably large fraction of their activity", and that Koyama et al do not suggest the degree of drying required to obtain a composition that is in a glassy state, are not convincing because the arguments can not be tied in with Appellants' claim language. Appellants' claims do not specify any particular % retention of activity or degree of drying, and patentability must be based upon claimed, not unclaimed, differences over the prior art. In any event, as discussed above, the retention of activity disclosed by Koyama et al for their drying process is fully consistent with the retention of activity achieved by Applicants for their drying process. Koyama et al suggest drying to a degree which is conventional in other prior art drying processes and to a degree which is consistent with achieving the degree of stability achieved in Koyama et al's specific examples.

At pages 18-19 of the Brief, Appellants argue that there are numerous process parameters not disclosed by Koyama et al which would require experimentation, and that an invitation to experiment is not sufficient to support an obviousness rejection. The examiner agrees that there are numerous unspecified process parameters in Koyama et al, but this is true about every

scientific publication. Koyama et al require experimentation, but there is a reasonable expectation of success because Koyama et al teach that such procedures "are feasible in the invention" (column 2, line 54). Further, the determination of operable and optimal process times, pressures, and temperatures is well within the ability of one of ordinary skill in the art because these are the fundamental variables which govern any drying process and would be routinely determined by one of ordinary skill in the art. Applicants' citation to In re Dow Chemical Co., 5 USPQ2d 1529 (Fed. Cir. 1988) is noted. As stated in Dow at page 1532, "There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure." This reason or suggestion is provided in Koyama et al itself, i.e. it is prima facie obvious to practice processes which a reference discloses and claims are useful for producing the reference's product. There is a reasonable expectation of success in the art for the reasons discussed above.

With respect to contention (7), Appellants did not invent immunoglobulins or blood clotting factors. These are all known substances which like all chemicals have to be stored and have to be stored in such a manner so as to maintain their activity. Because Koyama et al is applicable to all proteinaceous substances which exhibit a bioactivity in vivo, it would have been obvious to use the process of Koyama et al to store these particular proteinaceous substances. [With respect to the enzyme cofactors, nucleosides, nucleotides, etc., because the rejected claims are not limited to these particular materials, it is not relevant that Koyama et al do not suggest their drying and storage.]

With respect to contention (8), Koyama et al describe conventional drying procedures at reduced pressure and a temperature "below 30°C" (see column 2, line 54, and claim 6). At such

temperatures, there is at best minimal heating involved. Further, the disclosed temperature range renders prima facie obvious the determination of optimum temperatures within the disclosed temperature range, which includes those at which no heating occurs.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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December 4, 2003

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